More than consent for ethical open-label placebo research

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ABSTRACT

Recent studies have explored the effectiveness of open-label placebos (OLPs) for a variety of conditions, including chronic pain, cancer-related fatigue and irritable bowel syndrome. OLPs are thought to sidestep traditional ethical worries about placebos because they do not involve deception: with an OLP, patients or subjects are told outright that they are not given an active substance. As deception is framed as the primary hurdle to ethical placebo use, the door is ostensibly opened to ethical studies of OLPs. In this article, I suggest that even though OLPs seemingly do not involve deception, there are other ethical considerations in their clinical investigation and subsequent use. Research ethics often focusses on informed consent—of which, deception and honesty are a piece—as a means to justify research practices with human subjects. Yet, it is but one of the ethical considerations that should be taken into account. With research into placebo effects in particular, I argue that the history of clinical placebo use grounds special considerations for OLP research that go beyond respect for the autonomy of individual patients through informed consent and encompass structural concerns about the type of patient for whom a placebo has historically been thought appropriate.

PLACEBOS, THE PLACEBO EFFECT AND OPEN-LABEL PLACEBOS

The word 'placebo' is used in a variety of ways. In the clinical context, a placebo might be used to 'placate' a patient, as when a non-active substance (a 'pure' placebo) is given instead of an active substance, or an active substance (an 'impure' placebo) is used in a non-traditional way (eg, aspirin), to calm or satisfy a patient.[1] If the goal of this clinical use is not just to placate the patient such that they leave, but to invoke the placebo effect to benefit the patient, then the placebo is used as treatment. The placebo effect is generally understood as the range of potential therapeutic physiological and psychological responses following the clinical encounter, responses which may not be directly attributable to the use of a specific placebo mechanism (such as a pill or an exercise regimen) and may result from features of the clinical encounter itself.[2 3]

While the placebo effect can be measured, its mechanisms, whether psychological, neurobiological or otherwise, are disputed. Administering a deceptive placebo is generally considered unethical, as I explain in more detail in the next section.[i1]

One reason for the interest in open-label placebos (OLPs), is that they aim to invoke the beneficial effects of placebos without deception. With an OLP, patients or subjects are told outright that they are given a placebo.[4 5] OLP studies hypothesise that placebos can be effective even when there is complete transparency about what the participants are given.[6–9ii] These studies seek to show the effectiveness of OLPs for a variety of conditions, and to shed light on the mechanisms by which they occur, from adherence to the ritual of pill-taking, to the care received from the medical team, to behavioural conditioning and so on. OLPs are often described as ethically permissible, since they do not require deception for their effect,[10–13] although some dispute the claim that deceptive placebos are unethical.[14 15]

OLPs have been studied for a variety of conditions: chronic pain, irritable bowel syndrome (IBS), migraines, attention deficit hyperactivity disorder (ADHD), depression, cancer related fatigue, allergic rhinitis, wound healing and so on.[4 6–9 16–19] Other than wound healing, these are all conditions that have significant subjective symptoms. Indeed, it has been suggested that placebos have health benefits for many conditions, 'especially those with subjective symptoms'.[13] This does not mean that these conditions are thought to be completely subjective. Rather, they have both objectively assessable physical symptoms and symptoms that are subjectively characterised. For example, a patient with allergic rhinitis might have both the objectively observable physical symptom of a running and swollen nose, and the subjectively characterised symptom of itching and burning in the nose.

Some OLP studies have found that they are most effective for conditions in which psychological, social or contextual factors influence symptomatology. With this in mind, most effective OLP studies explicitly tell participants to expect benefit.[19 20] One of the earliest cited OLP studies was in 1965, in which 'neurotic' patients (patients with depression) were given a placebo and told that

[i]The placebo effect can be distinguished from the placebo response, which is the measured change of status of participants in the control arm of a randomised controlled trial (RCT). The use of a placebo as a control in a RCT is controversial for different reasons than the use of a placebo as treatment or placation in clinical care: deception is not an issue in RCTs. For this reason, ethical issues with using placebos in RCTs will be set aside for the purposes of this paper.

[ii]In this paper, I bypass the question of what actually causes the placebo effect. The ethical question here is not whether the placebo effect is due to expectations, physician-patient relationship, ritual or otherwise, but why certain conditions are thought to be appropriate applications for open-label placebos (OLPs).

it might help them, leading to a positive effect for 13 of the 14 participants.[21]

One of the first contemporary studies of OLPs, published in 2010, used a 3-week randomised controlled trial (RCT) to compare the administration of a placebo to a no treatment control arm in 70 participants with IBS. All participants were read the following script before being distributed into the two arms of the study and they were told which arm they were in:

(1) the placebo effect is powerful, (2) the body can automatically respond to taking placebo pills like Pavlov's dogs who salivated when they heard a bell, (3) a positive attitude helps but is not necessary, and (4) taking the pills faithfully is critical.[4]

The study found clinically meaningful symptom improvement in the OLP arm compared with the no treatment control arm (in the existing RCTs of OLPs, the placebo arm of the study is a no treatment arm).[20] An investigation of OLPs for chronic back pain in 2016 followed a similar methodology and found a comparable effect.[8] In a recent meta-analysis of OLP studies, four out of the five studies analysed included a similar description explaining the potential benefits of the placebo effect and all identified a positive clinical effect, although the authors express caution given the small number of studies and the fact that patients were explicitly told that placebos could have a positive outcome, thus influencing their beliefs and expectations.[20] These studies and others have led to speculation that perhaps the placebo effect derives not from any particular placebogenic intervention, such as a tablet or a cream, but from the expectations set in the clinical encounter.

Alia Crum hypothesises that the placebo effect occurs via beliefs or 'mindset'. In her definition, the placebo effect is any effect not attributed to an actual drug or remedy, but to the patient's mindset, composed of mindless beliefs and expectations.[22] Mindset encompasses elements of the psychosocial context of treatment, including expectations and beliefs.[23] Her work has shown that when participants' perception of an activity changes, the outcome of that activity can change. In Crum's research, shifting participant mindset has had both subjective and objective outcomes. In one study, participants who had been informed that their daily work was a form of beneficial exercise perceived themselves as getting more exercise *and* exhibited changes in weight, blood pressure, body fat and body mass index.[22] A similar study, not conducted by Crum, found that when healthcare providers exhibited certain interpersonal characteristics, such as warmth and competence, in setting expectations for benefit from a placebo (in this case, an allergy cream), the placebo effect was enhanced.[24] Crum has summarised that the placebo is 'a powerful demonstration of expectation and social context to produce physiological changes in the body'.[23]

Other OLP studies dispute Crum's account, suggesting that the placebo effect depends on more than mindset. An RCT of OLPs for allergic rhinitis compared OLPs with positive information against a no treatment control arm, and then compared OLPs with positive information to OLPs with no information. The results suggest that the positive effect of the OLP is not dependent on the information given; the placebo effect was found in both the positive information and no information groups. They thus conclude that it is unlikely that the positive results of OLPs come from expectancy mechanisms alone, although they note the small participant number (46) as a limitation.[19]

It is also unclear whether OLPs can modulate objective symptoms, as Crum's work suggests. A 2018 study of an OLP (tablets) for wound healing found no significant difference between the OLP and control conditions for percentage of wound healed, an objectively measured physiological outcome and not a subjective symptom.[25] Likewise, a 2017 study of an OLP (a cream) for analgesia found that the OLP group, when provided with a rationale for why a placebo might work for pain tolerance, experienced decreased subjective pain ratings but no change in objective pain tolerance measurements.[17]

As the explanation of OLP research above highlights, the field is still in relative infancy, both in terms of proving the effectiveness of OLPs for a variety of conditions and explaining the mechanism of the placebo effect. While studies of OLPs are generally supported, there have been few calls for the use of OLPs in clinical practice, at least not yet. This is largely due to the need for more studies—without research supporting the effectiveness of OLPs for particular conditions, they are still an investigative form of therapy. Nevertheless, OLPs have garnered significant interest in the popular imagination, perhaps due to the condemnation of deceptive placebos in clinical care, the ethical debate over the use of placebos in clinical research, and the interest in treatments that highlight the mind-body connection and provide relief without significant expense or side effects.[iii]

Placebos, the placebo effect and OLPs have also attracted significant ethical discussion, although deceptive placebos get the lion's share of interest. In the next section, I briefly review existing ethical analyses of OLPs in the context of the ethics of placebos more generally, before suggesting that there are more ethically significant dimensions to OLP studies than the current conversation evinces.

PLACEBOS AND THE ETHICS OF DECEPTION

Ethical analyses of OLP studies have focussed on informed consent as the primary means to determine the ethical permissibility of the study.[12 13] This reflects the focus on deception, which impedes informed consent, within the ethical debate on placebo use more broadly.[11 13–15 26] Few papers consider the ethics of placebo use as treatment outside of this individualistic focus on informed consent and deception.[5 27]

The ethical problem with deceptive placebo use is that it is paternalistic—it is based on the provider's assumption that they know better than the patient what is in the patient's best interests, and that acting on that superior knowledge requires acting without the patient's consent.[iv] This is the case when placebos are used for placation or treatment.

When used to placate, the provider assumes that the patient is wrong about what they need and that the provider has the accurate interpretation. This is paternalistic, insofar as it privileges the provider's judgment that the patient is imagining the symptoms or seeking attention. The assumption the provider makes is that, what the patient says they want is different from what the patient, in fact, needs. While the patient describes a condition that needs to be treated, the provider judges that the patient will be satisfied if they get something—anything—from them.

When used as treatment, the provider assumes that while the patient's self-report is accurate, deception is necessary for benefit.[28] This use of a deceptive placebo is slightly different from that of placation. In the case of a deceptive placebo for treatment, the hypothesis is that the patient does actually have a

[iii] http://www.nbcnews.com/video/nightly-news/40787382; https://www.sciencedaily.com/releases/2010/12/101222173033.htm; https://www.forbes.com/sites/daviddisalvo/2016/10/25/can-the-placebo-effect-really-work-without-deception-may-be-maybe-not/#5fe249ee2d0f

[iv] There is a rich philosophical discussion on the motivations behind paternalism and what makes paternalistic actions wrong. Here I am necessarily offering a more limited depiction.

medical condition and that the placebo effect can be helpful for that condition. Using deceptive placebos as treatment relies on the assumption, not accepted by all, that the mechanism of the placebo effect is psychosomatic—by thinking that they are being treated, some patients may actually become well.[11 29]

Proponents of OLPs depend on this framing of deception as the core ethical issue with placebos, arguing that, since OLPs do not require unethical deception, 'ethical objections to placebo use lose their force'.[30] This paves the way for research into OLPs as treatments, based on the argument that, if participants are informed that they are given a placebo, there is no ethical transgression because no deception is involved. Indeed, ethical analyses of OLPs in particular, and apart from deceptive placebos, come to precisely this conclusion: as long as participants are adequately informed about what an OLP is and how it is thought to work, there is no significant ethical issue.[12 31]

While it is surely prudent to begin the ethical discussion of OLPs with concerns about deception, there are other ethical considerations in their clinical investigation and subsequent use. Research ethics often focusses on informed consent—of which deception and honesty are a piece—as a means to justify research practices. Yet, it is but one of the ethical considerations that should be taken into account. While informed consent may be necessary for ethical research, it is not sufficient: arguably, ethical research with human subjects also must have social value, scientific validity, fair subject selection, independent review and a favourable risk-benefit ratio.[32] This means that ethical research practices ought not to be judged solely by the degree to which they respect participants' autonomy and balance benefits with harms, but by their accordance with our understanding of just social institutions. While justice has been traditionally understood in bioethics as the equitable distribution of benefits and burdens, in the following sections, I ground my argument in recent developments of philosophical theories of justice. These theories emphasise the importance of pursuing justice by targeting structural injustices,[33] of which epistemic injustices are a particularly thorny form.[34]

Targeting structural injustices, roughly, requires drawing attention to (and remediating) practices that privilege some social groups over others based on explicit or implicit assumptions about the social value or capabilities of that group. These injustices are epistemic when they involve assumptions about social groups' capacities as knowers, or as knowledge producers. Epistemic injustices are often based in assumptions that some groups' testimony is not legitimate, perhaps because they are judged to be cognitively unreliable or emotionally unstable.[35] Using these theories as groundwork, I argue that the history of clinical placebo use requires special considerations for OLP research that go beyond respect for individual patients through informed consent and encompass structural concerns about the type of patient for whom a placebo has historically been thought appropriate. In particular, I draw attention to testimonial injustices in historically deceptive placebo use that are entwined with paternalism, such that the rejection of some patients' capacities as knowers is used to justify actions in their best interests.

PATERNALISM AND INJUSTICE IN PLACEBO USE

Patients' beliefs, expectations and affective states seem to have a measurable effect on the outcome of placebo interventions, whether they are deceptive or not and whether they use physical interventions such as a pill, informational interventions such as expectations of benefit, or affective interventions such as the warmth of the provider. In acknowledging that placebo effects have a substantial subjective component, studies of OLPs build—for better or worse—on the assumptions that underlie historical uses of placebos for clinical purposes.

Historically, placebos were used when patients were suspected of inaccurately reporting their symptoms or making up symptoms where there were none. In a 1953 article about placebo use, the author points out that, 'some patients are so unintelligent, neurotic or inadequate as to be incurable, and life is made easier for them by a placebo. It has been said that the use of placebos is in inverse ratio to the combined intelligences of patient and doctor'.[36] In a 1955 article, Henry Beecher describes placebos as 'a medicine given more to please than to benefit the patient'.[37] Beecher continues to specify that placebos have among their clinical purposes: 'a psychological instrument in the therapy of certain ailments arising out of mental illness as a resource of the harassed doctor in dealing with the neurotic patient' and 'as a device for eliminating bias not only on the part of the patient but also, when unknown, on the part of the observer', in addition to the roles of placebos in research.[37] Thus placebos have been a tool both for providers to seek relief from 'neurotic patients' and for providers to suss out the real effects of therapy from imagined effects rooted in bias (such as a clinician's belief that an intervention must be effective).

Outside the research context, the premise behind placebos' historical clinical use is that they are appropriate for patients whose personal histories are unreliable, who are emotionally motivated and seeking comfort, or whose lives are missing something that a placebo might help. These motivations assume an unequal knowledge base between the patient and the provider—the patient is mistaken or confused, and the provider can see things accurately so as to help the patient. These motivations need not be malicious, but are often beneficent. In Beecher's words again, "the great power of placebos provides one of the strongest supports for the view that drugs are capable of altering subjective responses and symptoms and do so to an important degree through their effect on the reaction component of suffering."[37] The goal of placebo use is a good one: to benefit the patient by relieving suffering. As mentioned above, when administered deceptively, this beneficent motivation for sidestepping consent is the very core of paternalism.

OLPs, while they are not deceptive, might not escape the spectre of paternalism in medicine so easily. Arguably, the essence of paternalism in medicine is the assumption that providers know better than patients the true state of their condition and can judge which interventions will be in their best interests. Recent philosophical work has focussed on how this imbalance in epistemic power—that is, a difference in whose knowledge is seen as legitimate—leads to what is known as testimonial injustice, a form of epistemic injustice. Testimonial injustice occurs when individuals' testimony about their experiences (in this case, their experiences of illness) are assumed to be unreliable or imagined, and thus less credible or legitimate. Recently, philosophers have argued that testimonial injustice is a particularly entrenched form of structural injustice in medicine.[35] Healthcare practices privilege certain forms of testimony and evidence over others, such as providers' third-person descriptions of their patients over patients' first-person reports, and can be based on social constructions of illness that delegitimise patients' experiences.

Historically, members of certain social groups have been more liable to be subject to this assumption by medical providers than others.[38–42] Members of these social groups are treated unjustly when their testimony about their experience is judged to be unreliable or illegitimate by members of a privileged or dominant group. As Miranda Fricker has argued, epistemic injustice occurs

when dominant social groups are allowed to define the concepts or write the narratives about the experience of other social groups, thus creating institutional conditions of domination.[34] In medicine, this has historically occurred both by delegitimising the testimony of some social groups about their embodied experience and simultaneously legitimising the medical interpretation of this experience. Miller and Colloca note this concern in their ethical evaluation of placebos, observing that using a placebo can medicalise situations that are social or environmental.[31]

In the case of women, the most familiar example of this may be hysteria, a general term for mental illness which was used to describe women (and occasionally men) in the 19th century and which is often cited as an example of the medical profession's dismissal of the material reasons for patients' unrest.[43 44] Accounts of hysteria were based in negative cultural stereotypes of women as more emotional and less rationally grounded than men, which allowed medical professionals (almost all of whom were men) to depict themselves as solving a problem that women were helpless to solve themselves. While the problematic diagnosis of hysteria has disappeared from medical use, the disbelief and devaluation of women's experiences has not, as evidenced by the continued use of medical practices to monitor women's bodies and control their behaviour, especially during motherhood.[38–40] This is not unique to women but is also the case with other social groups who have been systematically devalued and delegitimised in American society, such as African slaves, whose 'desire to run away' was pathologised as drapetomania by Samuel A Cartwright in 1850.[44]

Due to these patterns of testimonial injustice in medicine, medical professionals and ethicists ought to be wary of the proposal that a condition can be treated with a placebo. As cited above, placebos have been thought appropriate for patients whose symptoms result from their own neuroses. Women, racial and ethnic minorities, persons with disabilities and others have been told that their pain must not really exist physically, that it must be in their head and that it must be a manifestation of some underlying emotional distress. The ethical question is whether OLPs themselves contribute to patterns of disbelief of patient narratives by suggesting that a placebo—historically, a problematic and unevenly applied intervention—is an appropriate form of treatment. Even though OLPs are not deceptive, it may be more difficult to escape the patterns of paternalism and testimonial injustice in placebos than has been imagined.

Currently, women comprise the majority of participants in many studies of OLPs, such as in the case of IBS,[18] asthma,[45] chronic low back pain,[8] chronic rhinitis[19] and cancer-related fatigue.[9] Alia Crum's ground-breaking research on mindset and exercise enrolled only female participants.[22] Furthermore, OLPs are deemed ethically permissible for conditions that predominantly affect women, such as chronic fatigue,[46] IBS,[47] major depressive disorder[48] and migraine.[49] To my knowledge, ADHD is the only disorder for which OLPs have been studied that is more prevalent in men than women.[50]

The use of OLP studies for conditions that primarily affect women is striking, especially given recent awareness of ologanalgesia—the undertreatment of pain—for women compared with men, and for members of minority racial and ethnic groups.[51 52] This suggests that disbelief of the reality of certain social groups' symptoms—the underlying motivation for much placebo use—remains a significant force in medicine. In this context, testing OLPs for conditions that predominantly affect women begins to seem more insidious, because it risks exacerbating an existing social tendency to disbelieve the testimony of women and other minorities about the physiologically-grounded reality of their own symptoms. This is in contrast to conditions with a large subjective component that primarily affect men, such as erectile dysfunction (ED). To my knowledge, no study has investigated OLPs for ED, although a recent meta-analysis suggests that placebos may be associated with ED improvement.[53]

In the context of an environment in which a woman's symptoms are more likely than a man's to be assumed misreported, psychosomatic or imaginary, the focus on investigating OLPs for conditions that primarily affect women and the current frequency of enrolling a majority of female participants in OLP studies risks a vicious cycle in which OLP studies reinforce assumptions about the primarily subjective nature of women's symptoms. This is not to say that these conditions do not have a subjective component, but that an unequal emphasis in OLP research on women's conditions implies that it is women's conditions that are primarily subjective. When women also make up the majority of participants in these studies, then the positive outcomes could be interpreted as reflecting the suggestibility of women in studies investigating the placebo effect through expectation, belief, and other psychological mechanisms.

Ethicists and researchers ought to be concerned about this imbalance in OLP research, especially given the history of deceptive placebo use in clinical care and the assumptions about patients' testimony that such use relied on. These assumptions not only render some patients' testimony less credible, but they serve to ground paternalistic behaviour in which decisions are made for patients, ostensibly in their interest, but without their consent. The ethical lens through which to view this research agenda ought not be consent alone, as it has been up until now. Rather, in analysing research agendas that are grounded in social practices which accord power and legitimacy to some social groups over others, ethicists ought to pay special attention to questions of structural injustice, of which epistemic injustice is a particularly entrenched form.

MORE THAN CONSENT IN THE ETHICS OF OPEN-LABEL PLACEBOS

In their now classic essay on clinical research ethics, Emanuel, Wendler and Grady write,

"What makes clinical research ethical? Informed consent is the answer most US researchers, bioethicists and institutional review board (IRB) members would probably offer. This response reflects the preponderance of existing guidance on the ethical conduct of research and the near obsession with autonomy in US bioethics. While informed consent is necessary in most but not all cases, in no case is it sufficient for ethical clinical research."

They identify seven ethical requirements of ethical clinical research. Apart from informed consent, the other six are social or scientific value, scientific validity, fair subject selection, favourable risk benefit ratio, and respect for potential and enrolled subjects.[32] They emphasise that informed consent is not the sole criterion of ethical research, as is the case in research that takes advantage of economic disparities, research with individuals who are incarcerated, research that will not advance scientific understanding and so on. In these types of cases, even though participants may consent to the research, underlying issues of scientific validity or fair subject selection will not be addressed by consent alone.

While informed consent has been the focus of ethical analyses of OLP research, this focus is most relevant for the deceptive use of placebos for clinical treatment. When placebos are studied or administered open label, this focus on deception

versus transparency as the primary plane of ethical analysis need not hold.[v] As argued above, the assumptions that physicians make about when patients are giving reliable testimony can be grounded in biases and power imbalances between social groups. When OLPs are then investigated with a majority of participants from social groups that have been historically disbelieved and devalued and for conditions that affect those social groups primarily, this runs the risk of reinforcing these imbalances, even if they are not explicitly grounded in assumptions about social worth.

The historical injustices experienced in medicine by women and minority patients, coupled with the systemic disbelief that many of these patients are already likely to experience as in the case of ologanalgesia, is just another guise of paternalism. When clinicians give a patient a placebo because they expect some benefit that the patient is not able to anticipate, based on the belief that they know better than their patients what their experience is like, or based in the suspicion that a patient's testimony about their experience is unreliable or inaccurate, they make a paternalistic judgment. Likewise, when researchers believe that some patients' experiences can be studied through a psychogenic mechanism such as a placebo rather than a physiological 'little blue pill', they act paternalistically, even if participants in these studies have given consent. As philosophers have recently argued, ethically problematic paternalism need not explicitly violate consent if the motive of the intervention is an infantilisation or disbelief of the testimony of the person who is paternalised.[54 55]

While paternalism is not inherently unethical, the form that paternalistic behaviour has taken in medical research and practice has frequently been problematic, based on the assumptions highlighted above about who determines benefit for whom and how that benefit is pursued. Especially with research as opposed to clinical practice, where practices are meant to universalise across populations and not to be specific to one particular patient, there is the need for excess caution about the problematic assumptions about the experiences and testimony of marginalised groups that render that research agenda plausible.

This is not to say that OLP research has no value. It should be praised for its progressive approach to the mind-body relationship and its advancement of research that can improve human lives without necessarily generating revenue for novel designer interventions. Studies of the placebo effect have also increased awareness of issues of equity and justice in how healthcare is administered by professionals, not just whether it is materially available.[27] Research on OLPs has promise across a broad range of conditions. However, it is essential to acknowledge and to counter the problematic assumptions about individuals for whom placebos are appropriate as the OLP research agenda unfolds.

To avoid replicating these patterns of injustice that relate to placebo use, I propose that OLP studies investigate conditions that affect men and women equally or men predominantly, that there be equal enrolment of male and female participants in OLP studies for conditions that affect genders equally, and that interventions such as OLPs, which primarily target psychogenic mechanisms of medical conditions, be investigated alongside interventions that target physiological mechanisms of those same conditions. The first two proposals would help to balance the gender representation in studies of OLPs, ensuring that OLPs are investigated for conditions that affect both genders and are neither unevenly targeted towards women's conditions nor are investigated with only female participants. As I have argued, this uneven gender distribution in OLP studies problematically reflects and reinforces assumptions about who experiences the placebo effect most forcefully and why. These suggestions would also hold, should OLP studies be found to have uneven representation with respect to other social groups who have historically been subject to the paternalistic assumptions of placebo use, such as racial and ethnic minorities.

The third proposal, that clinical research balances studies investigating psychogenic and physiological pathways for relief of symptoms is meant to ensure that assumptions about conditions' mechanisms do not influence research funding and study priorities without proper investigation. One of the most interesting dimensions of OLP research is the extent to which it highlights how little we still know about the mechanisms by which symptoms are relieved or exacerbated.

In conclusion, OLP studies ought to both acknowledge the problematic history of placebo use and take steps to mitigate this history's effects. Without implementing these and other means of rectifying the scepticism about certain groups' experiences that is embedded in the research programme, OLP research may find itself reflecting and reinforcing problematic assumptions underlying historical placebo use, forestalling progress in making placebos more ethically viable.

[v]Although in some cases it might, as with concerns that the nature of OLPs are not accurately described.

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